Complete Summary

GUIDELINE TITLE

Diagnosis and treatment of gestational trophoblastic disease.

BIBLIOGRAPHIC SOURCE(S)

American College of Obstetricians and Gynecologists (ACOG). Diagnosis and treatment of gestational trophoblastic disease. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2004 Jun. 13 p. (ACOG practice bulletin; no. 53). [49 references]

GUIDELINE STATUS

This is the current release of the guideline.

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SCOPE

DISEASE/CONDITION(S)

Gestational trophoblastic disease (gestational trophoblastic neoplasia, gestational trophoblastic tumor), including:

- Hydatidiform moles
- Invasive moles
- Gestational choriocarcinomas
- Placental site trophoblastic tumors

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Obstetrics and Gynecology
Oncology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To aid practitioners in making decisions about appropriate obstetric and gynecologic care
- To address current evidence regarding the diagnosis, staging, and management of gestational trophoblastic disease

TARGET POPULATION

Women of reproductive age with gestational trophoblastic disease

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Evaluation of symptoms of gestational trophoblastic disease (e.g., abnormal bleeding)
2. Measurement of beta-human chorionic gonadotropin levels
3. Chest x-ray
4. Ultrasound
5. Other laboratory tests
6. Serial hCG determinations
7. Classification and staging of disease

Management/Treatment

1. Suction dilatation and curettage (D&C)
2. Methotrexate
3. Multiagent chemotherapy (methotrexate, dactinomycin, chlorambucil, cyclophosphamide, cisplatin, etoposide)
4. Hysterectomy
5. Counseling on use of oral contraceptives

MAJOR OUTCOMES CONSIDERED

- Predictive value of clinical signs and symptoms
- Response rate to therapy

- Recurrence rate
- Rate of preservation of fertility
- Maternal morbidity and mortality
- Infant morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and February 2004. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Analysis of available evidence was given priority in formulating recommendations. When reliable research was not available, expert opinions from obstetrician–gynecologists were used. See also the "Rating Scheme for the Strength of Recommendations" field regarding Grade C recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A — Recommendations are based on good and consistent scientific evidence.

Level B — Recommendations are based on limited or inconsistent scientific evidence.

Level C — Recommendations are based primarily on consensus and expert opinion.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practice Bulletins are validated by two internal clinical review panels composed of practicing obstetrician-gynecologists generalists and sub-specialists. The final guidelines are also reviewed and approved by the American College of Obstetricians and Gynecologists (ACOG) Executive Board.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of evidence (I-III) and levels of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

The following recommendations are based on good and consistent scientific evidence (Level A):

- In women of reproductive age with abnormal bleeding or symptoms that could be caused by a malignancy, beta-human chorionic gonadotropin (beta-hCG) levels should be evaluated to facilitate early diagnosis and treatment of gestational trophoblastic disease.
- In patients with molar pregnancy, the preferred method of evacuation is suction dilation and curettage (D&C). After molar evacuation, all patients should be monitored with serial hCG determinations to diagnose and treat malignant sequelae promptly.
- Oral contraceptives have been demonstrated to be safe and effective during posttreatment monitoring based on randomized controlled trials.
- Women with nonmetastatic gestational trophoblastic disease should be treated with single-agent chemotherapy.
- For women with nonmetastatic gestational trophoblastic disease, weekly doses of 30 to 50 mg/m^2 of intramuscular methotrexate has been found to be the most cost-effective treatment when taking efficacy, toxicity, and cost into consideration.
- Women with metastatic gestational trophoblastic disease should be referred to specialists with experience treating this disease.
- Women with high-risk metastatic disease should be treated with multiagent chemotherapy. This includes triple therapy with methotrexate, dactinomycin, and either chlorambucil or cyclophosphamide. More recent regimens further incorporate etoposide with or without cisplatin into combination chemotherapy.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- False-positive test results should be suspected if hCG values plateau at relatively low levels and do not respond to therapeutic maneuvers, such as methotrexate given for a presumed persistent mole or ectopic pregnancy.
- Serial quantitative serum hCG determinations should be performed using a commercially available assay capable of detecting beta-hCG to baseline values (<5 milli-international units per milliliter [mIU/mL]). Ideally, serum hCG levels should be obtained within 48 hours of evacuation, every 1 to 2

weeks while elevated, and then at 1 to 2 month intervals for an additional 6 to 12 months.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- Abnormal bleeding for more than 6 weeks following any pregnancy should be evaluated with hCG testing to exclude a new pregnancy or gestational trophoblastic disease.
- In compliant patients, the low morbidity and mortality achieved by monitoring patients with serial hCG determinations and instituting chemotherapy only in patients with postmolar gestational trophoblastic disease outweighs the potential risk and small benefit of routine prophylactic chemotherapy after evacuation of a molar pregnancy.
- Serious complications are not uncommon in women with a uterus size greater than a 16-week gestation, so they should be managed by physicians experienced in the prevention and management of complications.
- Patients for whom initial therapy for nonmetastatic or low-risk metastatic disease fails and those with high-risk malignant gestational trophoblastic disease should be managed in consultation with individuals or facilities with expertise in the complex, multimodality treatment of these patients.

Definitions:

Grades of Evidence

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Levels of Recommendations

Level A — Recommendations are based on good and consistent scientific evidence.

Level B — Recommendations are based on limited or inconsistent scientific evidence.

Level C — Recommendations are based primarily on consensus and expert opinion.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and treatment of gestational trophoblastic disease

POTENTIAL HARMS

- Dilation and curettage (D&C) should be avoided to treat invasive hydatidiform mole to prevent morbidity and mortality caused by uterine perforation.
- Biopsy of sites of metastases from malignant gestational trophoblastic disease is rarely necessary and may cause excessive bleeding.
- It is important to exclude the possibility of false-positive human chorionic gonadotropin (hCG) values before subjecting patients to hysterectomy or chemotherapy for gestational trophoblastic disease.
- Patients should have normal renal and liver functions before each treatment because methotrexate is excreted entirely by the kidney and can produce hepatic toxicity.
- More recent combination chemotherapy regimens for high-risk metastatic disease have incorporated etoposide with or without cisplatin into combination chemotherapy with high rates of success but with an increased risk for leukemia in survivors.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

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2004 Jun

GUIDELINE DEVELOPER(S)

American College of Obstetricians and Gynecologists - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Obstetricians and Gynecologists (ACOG)

GUIDELINE COMMITTEE

American College of Obstetricians and Gynecologists (ACOG) Committee on Practice Bulletins-Gynecology

SGO Education Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: None available

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 4500, Kearneysville, WV 25430-4500; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Early pregnancy loss: miscarriage and molar pregnancy. Atlanta (GA): American College of Obstetricians and Gynecologists (ACOG); 2002.

Electronic copies: Available from the American College of Obstetricians and Gynecologists (ACOG) Web site.

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 4500, Kearneysville, WV 25430-4500; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site.

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NGC STATUS

This NGC summary was completed by ECRI Institute on October 11, 2007. The information was verified by the guideline developer on December 3, 2007.

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